10/ 541,535

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 NEWS  1          Web Page URLs for STN Seminar Schedule - N. America
 NEWS  2  JAN 08  CHEMLIST enhanced with New Zealand Inventory of Chemicals
 NEWS  3  JAN 16  CA/CAplus Company Name Thesaurus enhanced and reloaded
 NEWS  4  JAN 16  IPC version 2007.01 thesaurus available on STN
 NEWS  5  JAN 16  WPIDS/WPINDEX/WPIX enhanced with IPC 8 reclassification data
 NEWS  6  JAN 22  CA/CAplus updated with revised CAS roles
 NEWS  7  JAN 22  CA/CAplus enhanced with patent applications from India
 NEWS  8  JAN 29  PHAR reloaded with new search and display fields
 NEWS  9  JAN 29  CAS Registry Number crossover limit increased to 300,000 in
                  multiple databases
 NEWS 10  FEB 15  PATDPASPC enhanced with Drug Approval numbers
 NEWS 11  FEB 15  RUSSIAPAT enhanced with pre-1994 records
 NEWS 12  FEB 23  KOREAPAT enhanced with IPC 8 features and functionality
 NEWS 13  FEB 26  MEDLINE reloaded with enhancements
 NEWS 14  FEB 26  EMBASE enhanced with Clinical Trial Number field
 NEWS 15  FEB 26  TOXCENTER enhanced with reloaded MEDLINE
 NEWS 16  FEB 26  IFICDB/IFIPAT/IFIUDB reloaded with enhancements
 NEWS 17  FEB 26  CAS Registry Number crossover limit increased from 10,000
                  to 300,000 in multiple databases
 NEWS 18  MAR 15  WPIDS/WPIX enhanced with new FRAGHITSTR display format
 NEWS 19  MAR 16  CASREACT coverage extended
 NEWS 20  MAR 20  MARPAT now updated daily
 NEWS 21  MAR 22  LWPI reloaded
 NEWS 22  MAR 30  RDISCLOSURE reloaded with enhancements
 NEWS 23  APR 02  JICST-EPLUS removed from database clusters and STN
 NEWS 24  APR 30  GENBANK reloaded and enhanced with Genome Project ID field
 NEWS 25  APR 30  CHEMCATS enhanced with 1.2 million new records
 NEWS 26  APR 30  CA/CAplus enhanced with 1870-1889 U.S. patent records
 NEWS 27  APR 30  INPADOC replaced by INPADOCDB on STN
 NEWS 28  MAY 01  New CAS web site launched

 NEWS EXPRESS  NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT
               MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.

 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
 NEWS LOGIN    Welcome Banner and News Items
 NEWS IPC8     For general information regarding STN implementation of IPC 8
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Enter NEWS followed by the item number or name to see news on that specific topic.

10/ 541,535

* * * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 14:11:00 ON 07 MAY 2007

=> file reg
COST IN U.S. DOLLARS

| | SINCE FILE ENTRY | TOTAL SESSION |
|---|---|---|
| FULL ESTIMATED COST | 0.21 | 0.21 |

FILE 'REGISTRY' ENTERED AT 14:11:10 ON 07 MAY 2007
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.


Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES: 6 MAY 2007 HIGHEST RN 934336-20-6
DICTIONARY FILE UPDATES: 6 MAY 2007 HIGHEST RN 934336-20-6

New CAS Information Use Policies, enter HELP USAGETERMS for details.

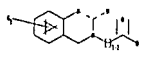
TSCA INFORMATION NOW CURRENT THROUGH December 2, 2006

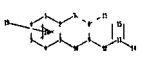
Please note that search-term pricing does apply when
conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document. For information
on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

=>
Uploading C:\Program Files\Stnexp\Queries\10541535.str





chain nodes :
11 12 13 14 15 19
ring nodes :

10/ 541,535

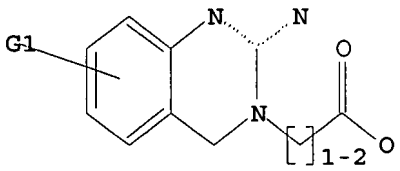
1 2 3 4 5 6 7 8 9 10
chain bonds :
8-11 9-12 12-13 13-14 13-15
ring bonds :
1-2 1-6 2-3 2-7 3-4 3-10 4-5 5-6 7-8 8-9 9-10
exact/norm bonds :
2-7 3-10 7-8 8-9 8-11 9-10 9-12 13-14 13-15
exact bonds :
12-13
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6
isolated ring systems :
containing 1 :

G1:H,X

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:CLASS 12:CLASS 13:CLASS 14:CLASS 15:CLASS 19:CLASS 20:Atom

L1 STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1 STR




G1 H,X

Structure attributes must be viewed using STN Express query preparation.

=> s l1 sample
SAMPLE SEARCH INITIATED 14:11:35 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 595 TO ITERATE

100.0% PROCESSED 595 ITERATIONS 9 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 10437 TO 13363
PROJECTED ANSWERS: 9 TO 360

L2 9 SEA SSS SAM L1

=> s l1 ful
FULL SEARCH INITIATED 14:11:42 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 11878 TO ITERATE

100.0% PROCESSED 11878 ITERATIONS 166 ANSWERS
SEARCH TIME: 00.00.01

10/ 541,535

L3 166 SEA SSS FUL L1

=> file zcaplus
COST IN U.S. DOLLARS SINCE FILE ENTRY 172.10 TOTAL SESSION 172.31
FULL ESTIMATED COST

FILE 'ZCAPLUS' ENTERED AT 14:11:49 ON 07 MAY 2007
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.


FILE COVERS 1907 - 7 May 2007 VOL 146 ISS 20
FILE LAST UPDATED: 6 May 2007 (20070506/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l3
L4 20 L3

=> d his

(FILE 'HOME' ENTERED AT 14:11:00 ON 07 MAY 2007)

FILE 'REGISTRY' ENTERED AT 14:11:10 ON 07 MAY 2007
L1 STRUCTURE UPLOADED
L2 9 S L1 SAMPLE
L3 166 S L1 FUL

FILE 'ZCAPLUS' ENTERED AT 14:11:49 ON 07 MAY 2007
L4 20 S L3

=> d l4 1- ibib abs hitstr
YOU HAVE REQUESTED DATA FROM 20 ANSWERS - CONTINUE? Y/(N):y

L4 ANSWER 1 OF 20 ZCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:385933 ZCAPLUS
DOCUMENT NUMBER: 144:370110
TITLE: Preparation of anagrelide hydrochloride
PATENT ASSIGNEE(S): AOP Orphan Pharmaceuticals A.-G., Austria
SOURCE: Austrian, 7 pp.
CODEN: AUXXAK
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|

10/ 541,535

| | | | | | |
|---|---|---|---|---|---|
| AT 412873 | B | 20050825 | AT 2004-273 | | 20040220 |
| AT 200400273 | A | 20050115 | | | |
| WO 2005080398 | A1 | 20050901 | WO 2005-AT32 | | 20050203 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: AT 2004-273 A 20040220
OTHER SOURCE(S): CASREACT 144:370110
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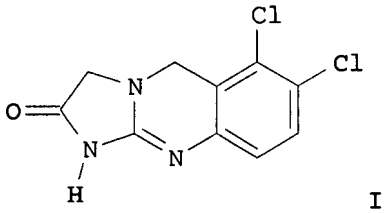


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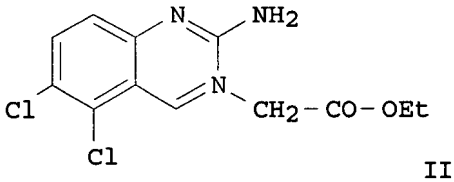


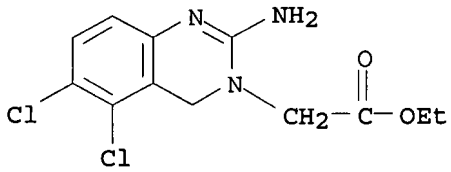

II

AB A process for the preparation of title compound I from 2,3-dichlorobenzaldehyde in 7-steps was disclosed. For example, NaHCO3 mediated cyclization of quinazolineacetic acid II afforded anagrelide in 80% yield.

IT 742010-46-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of anagrelide hydrochloride)

RN 742010-46-4 ZCAPLUS

CN 3(4H)-Quinazolineacetic acid, 2-amino-5,6-dichloro-, ethyl ester (9CI) (CA INDEX NAME)




L4 ANSWER 2 OF 20 ZCAPLUS COPYRIGHT 2007 ACS on STN

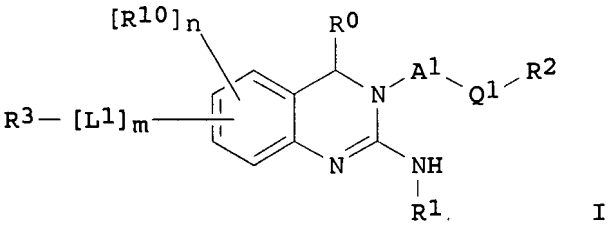
ACCESSION NUMBER: 2006:213433 ZCAPLUS
DOCUMENT NUMBER: 144:274294
TITLE: Novel 2-aminoquinazoline derivatives, their preparation and use as inhibitors of β-secretase for treating Alzheimer's disease and related disorders
INVENTOR(S): Bishoff, Francois Paul; Bracken, Mirielle; Pieters, Serge Marie Aloysius; Mercken, Marc Hubert; De Winter, Hans Louis Jos; Berthelot, Dieder Jean-Claude
PATENT ASSIGNEE(S): Janssen Pharmaceutica, N. V., Belg.
SOURCE: PCT Int. Appl., 369 pp.
CODEN: PIXXD2

10/ 541,535

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2006024932 | A1 | 20060309 | WO 2005-IB2595 | 20050808 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| US 2006079686 | A1 | 20060413 | US 2005-197608 | 20050804 |
| US 2006079687 | A1 | 20060413 | US 2005-197669 | 20050804 |
| US 2006178383 | A1 | 20060810 | US 2005-197615 | 20050804 |
| PRIORITY APPLN. INFO.: | | | US 2004-599810P P | 20040806 |
| | | | US 2004-599317P P | 20040806 |
| | | | US 2004-599811P P | 20040806 |

OTHER SOURCE(S): MARPAT 144:274294
GI

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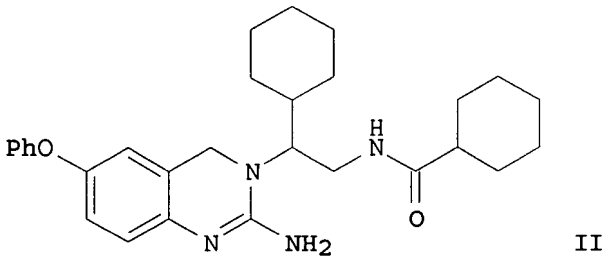



II

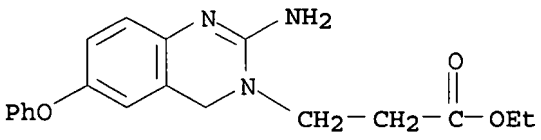
AB The invention is related to novel 2-amino-3,4-dihydro-quinazoline derivs. I [R0 = H, Me, CF3; R1 = H, OH, Me, Et, CF3, OEt, etc.; A1 = (un)substituted alkyl; Q1= O, S, CO, CS, NHCO, CONH, etc.; R2 = (un)substituted cyclo/alkyl, aryl, spiroheterocyclyl, etc.; m = 0-1; R3 = (un)substituted alk(en)yl, aryl, etc.; n = 0-3; each R10 = independently OH, halo, alkyl, alkoxy, etc.; with provisos] pharmaceutical compns. containing them and their use as inhibitors of β-secretase, also known as β-site cleaving enzyme and BACE, in the treatment of Alzheimer's disease and related disorders. E.g., a multi-step synthesis starting from

N-(tert-butoxycarbonyl)glycine Me ester and N,O-dimethylhydroxylamine•HCl was given for aminoquinazoline II. I inhibited β-secretase in 3 different assays.

IT 876763-94-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of 2-aminoquinazolines as β-secretase inhibitors for treating Alzheimer's disease and related disorders)

RN 876763-94-9 ZCAPLUS

CN 3(4H)-Quinazolinepropanoic acid, 2-amino-6-phenoxy-, ethyl ester (9CI) (CA INDEX NAME)




REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 20 ZCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:152738 ZCAPLUS
DOCUMENT NUMBER: 144:254142
TITLE: Novel 2-aminoquinazoline derivatives, their preparation and use as inhibitors of β-secretase for treating Alzheimer's disease and related disorders
INVENTOR(S): Baxter, Ellen; Bischoff, Francois Paul; Boyd, Robert; Braeken, Mirielle; Coats, Steven; Huang, Yifang; Jordan, Alfonzo; Luo, Chi; Mercken, Marc Hubert; Reynolds, Charles H.; Ross, Tina Morgan; Tounge, Brett A.; Schulz, Mark; De Winte, Hans Louis Jos; Pieters, Serge Maria Aloysius; Reitz, Allen B.
PATENT ASSIGNEE(S): Janssen Pharmaceutica, N.V., Belg.
SOURCE: PCT Int. Appl., 385 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2006017836 | A2 | 20060216 | WO 2005-US28191 | 20050808 |
| WO 2006017836 | A3 | 20060629 | | |
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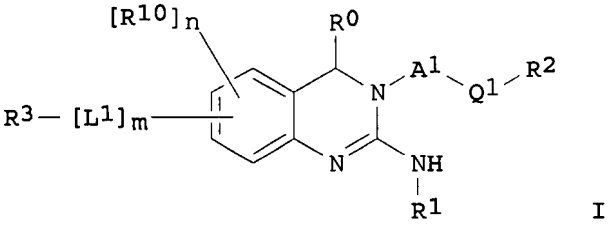
| RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| US 2006079686 | A1 | 20060413 | US 2005-197608 | 20050804 |
| US 2006079687 | A1 | 20060413 | US 2005-197669 | 20050804 |
| US 2006178383 | A1 | 20060810 | US 2005-197615 | 20050804 |

10/ 541,535

EP 1776349 A2 20070425 EP 2005-785256 20050808
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU
PRIORITY APPLN. INFO.: US 2004-599811P P 20040806
US 2004-599317P P 20040806
US 2004-599810P P 20040806
WO 2005-US28191 W 20050808
OTHER SOURCE(S): MARPAT 144:254142
GI



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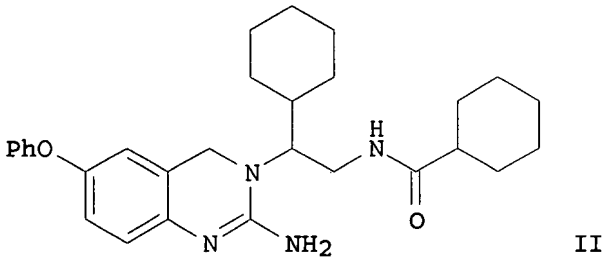


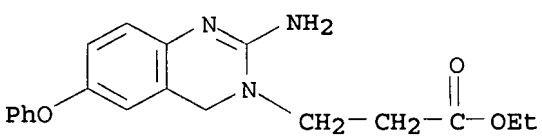
II

AB The invention is related to novel 2-amino-3,4-dihydro-quinazoline derivs. I [R0 = H, Me, CF3; R1 = H, OH, Me, Et, CF3, OEt, etc.; A1 = (un)substittued alkyl; Q1 = O, S, CO, CS, NHCO, CONH, etc.; R2 = (un)substituted cyclo/alkyl, aryl, spiroheterocyclyl; m = 0-1; L1 = O, S, SO, SO2, etc.; R3 = (un)substituted alk(en)yl, aryl, etc.; n = 0-3; each R10 = independently OH, halo, alkyl, alkoxy, etc.; with provisos] pharmaceutical compns. containing them and their use as inhibitors of β-secretase, also known as β-site cleaving enzyme and BACE, in the treatment of Alzheimer's disease and related disorders. E.g., a multi-step synthesis starting from N-(tert-butoxycarbonyl)glycine Me ester and N,O-dimethylhydroxylamine•HCl was given for aminoquinazoline II. I inhibited β-secretase in 3 different assays.

IT 876763-94-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of 2-aminoquinazolines as β-secretase inhibitors for treating Alzheimer's disease and related disorders)

RN 876763-94-9 ZCAPLUS

CN 3(4H)-Quinazolinepropanoic acid, 2-amino-6-phenoxy-, ethyl ester (9CI) (CA INDEX NAME)



L4 ANSWER 4 OF 20 ZCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:149827 ZCAPLUS
DOCUMENT NUMBER: 144:254141
TITLE: Novel 2-aminoquinazoline derivatives, their preparation and use as inhibitors of β-secretase for treating Alzheimer's disease and related disorders
INVENTOR(S): Baxter, Ellen; Boyd, Robert; Coats, Steve; Jordan, Alfonzo; Reitz, Allen; Reynolds, Charles H.; Scott, Malcolm; Schulz, Mark; De Winter, Hans Louis Jos
PATENT ASSIGNEE(S): Janssen Pharmaceutica, N.V., Belg.
SOURCE: PCT Int. Appl., 382 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2006017844 | A1 | 20060216 | WO 2005-US28340 | 20050808 |
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| US 2006079686 | A1 | 20060413 | US 2005-197608 | 20050804 |
| US 2006079687 | A1 | 20060413 | US 2005-197669 | 20050804 |
| US 2006178383 | A1 | 20060810 | US 2005-197615 | 20050804 |
| EP 1776350 | A1 | 20070425 | EP 2005-786778 | 20050808 |
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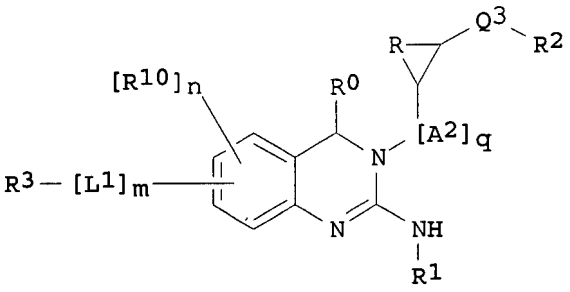
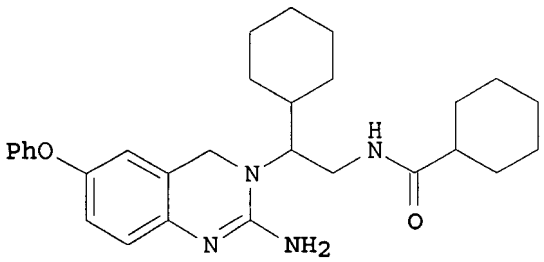
| | | | |
|---|---|---|---|
| PRIORITY APPLN. INFO.: | US 2004-599317P | P | 20040806 |
| | US 2004-599810P | P | 20040806 |
| | US 2004-599811P | P | 20040806 |
| | WO 2005-US28340 | W | 20050808 |

OTHER SOURCE(S): MARPAT 144:254141
GI



I



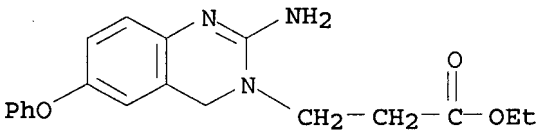
II

AB The invention is related to novel 2-amino-3,4-dihydro-quinazoline derivs. I [R0 = H, Me, CF3; R1 = H, OH, Me, Et, CF3, OEt, etc.; q = 0-1; A2 = (un)substituted alkyl; R = (un)substituted hetero/aryl, arylalkyl, hetero/cycloalkyl, partially unsatd. carbocyclyl, spiroheterocyclyl; provided that when q = 0; R is other than hetero/aryl; Q3 = O, S, CO, CS, OCO, etc.; R2 = (un)substituted cyclo/alkyl, aryl, spiroheterocyclyl, etc.; m = 0-1; L1 = O, S, SO, SO2, CO, NH and derivs., etc.; R3 = (un)substituted cyclo/alkyl, alkenyl, hetero/aryl, etc.; n = 0-3; each R10 = independently OH, halo, alkyl, alkoxy, etc.; with provisos] pharmaceutical compns. containing them and their use as inhibitors of β-secretase, also known as β-site cleaving enzyme and BACE, in the treatment of Alzheimer's disease and related disorders. E.g., a multi-step synthesis starting from N-(tert-butoxycarbonyl)glycine Me ester and N,O-dimethylhydroxylamine•HCl was given for aminoquinazoline II. I inhibited β-secretase in 3 different assays.

IT 876763-94-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of 2-aminoquinazolines as β-secretase inhibitors for treating Alzheimer's disease and related disorders)

RN 876763-94-9 ZCAPLUS

CN 3(4H)-Quinazolinepropanoic acid, 2-amino-6-phenoxy-, ethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 20 ZCAPLUS COPYRIGHT 2007 ACS on STN

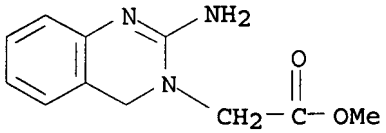
10/ 541,535

ACCESSION NUMBER: 2005:378803 ZCAPLUS
DOCUMENT NUMBER: 143:78149
TITLE: Base catalyzed intramolecular transamidation of 2-aminoquinazoline derivatives on solid phase
AUTHOR(S): Grover, Rajesh K.; Kesarwani, Amit P.; Srivastava, Gaurav K.; Kundu, Bijoy; Roy, Raja
CORPORATE SOURCE: Division of SAIF, Central Drug Research Institute, Lucknow, 226001, India
SOURCE: Tetrahedron (2005), 61(21), 5011-5018
CODEN: TETRAB; ISSN: 0040-4020
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 143:78149

AB A novel intramol. cycloelimination via transamidation on Rink Amide AM resin under mild basic conditions is presented. The methodol. led to the synthesis of an important class of cardiotonic agents: imidazo- and pyrimidoquinazolines from the corresponding 2-aminoquinazoline hydrobromide salt under mild basic conditions. NMR based titration studies revealed the role of hydrobromide as a mol. switch, which on removal triggers the cyclization of aminoquinazoline to tricyclic structures. The main advantage of transamidation under basic conditions over the TFA cleavage is the recyclability of the resin obtained after cycloelimination. This has been demonstrated by successive synthesis of four structurally diverse imidazoquinazolin-2-ones using the same batch of resin without any cross contamination.

IT 855005-11-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of imidazo- and pyrimidoquinazolines by base catalyzed intramol. transamidation of 2-aminoquinazolines on solid phase)

RN 855005-11-7 ZCAPLUS
CN 3(4H)-Quinazolineacetic acid, 2-amino-, methyl ester, monohydrobromide (9CI) (CA INDEX NAME)




● HBr

REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

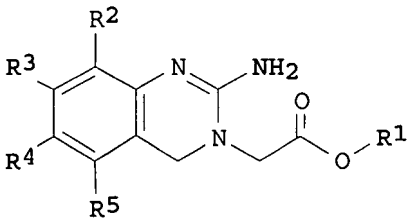
L4 ANSWER 6 OF 20 ZCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:587927 ZCAPLUS
DOCUMENT NUMBER: 141:117193
TITLE: 2-Amino-2H-quinazoline derivatives as prodrugs for the bronchdilator anagrelid
INVENTOR(S): Sachse, Rolf
PATENT ASSIGNEE(S): Chemisch-Pharmazeutisches Labor, Rolf Sachse GmbH, Germany
SOURCE: Ger. Offen., 7 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| DE 10301105 | A1 | 20040722 | DE 2003-10301105 | 20030109 |
| DE 10301105 | B4 | 20051124 | | |
| AU 2004203910 | A1 | 20040729 | AU 2004-203910 | 20040107 |
| CA 2512999 | A1 | 20040729 | CA 2004-2512999 | 20040107 |
| WO 2004063172 | A1 | 20040729 | WO 2004-EP54 | 20040107 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ | | | | |
| EP 1581506 | A1 | 20051005 | EP 2004-700454 | 20040107 |
| EP 1581506 | B1 | 20061129 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| JP 2006516565 | T | 20060706 | JP 2006-500528 | 20040107 |
| AT 346844 | T | 20061215 | AT 2004-700454 | 20040107 |
| US 2006148832 | A1 | 20060706 | US 2005-541535 | 20050709 |

PRIORITY APPLN. INFO.: DE 2003-10301105 A 20030109; WO 2004-EP54 W 20040107

OTHER SOURCE(S): MARPAT 141:117193

GI



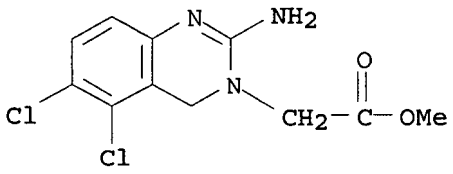
I

AB 2-Amino-2H-quinazolines I [R1 = alkyl; R2-R5 = H, Cl] are prodrugs for the bronchdilator anagrelid. They cyclize to anagrelid in basic medium. Thus, I [R1 = Me, R2, R3 = H, R4, R5 = Cl] was cyclized 100% in 0.1 M NaOH.

IT 70380-52-8 70380-54-0 70380-55-1
70381-75-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(2-amino-2H-quinazoline derivs. as prodrugs for the bronchdilator anagrelid)

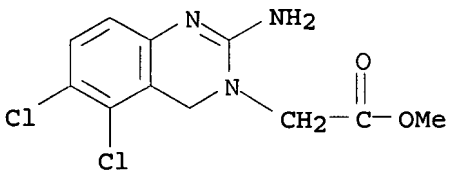
RN 70380-52-8 ZCAPLUS

CN 3(4H)-Quinazolineacetic acid, 2-amino-5,6-dichloro-, methyl ester, monohydrobromide (9CI) (CA INDEX NAME)



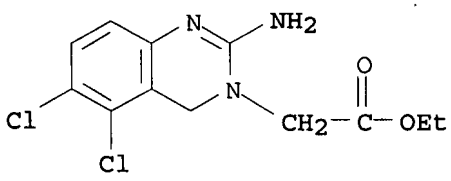
● HBr

RN 70380-54-0 ZCAPLUS
CN 3(4H)-Quinazolineacetic acid, 2-amino-5,6-dichloro-, methyl ester, monohydrochloride (9CI) (CA INDEX NAME)



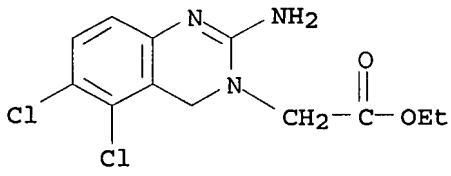
● HCl

RN 70380-55-1 ZCAPLUS
CN 3(4H)-Quinazolineacetic acid, 2-amino-5,6-dichloro-, ethyl ester, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 70381-75-8 ZCAPLUS
CN 3(4H)-Quinazolineacetic acid, 2-amino-5,6-dichloro-, ethyl ester, monohydrobromide (9CI) (CA INDEX NAME)



● HBr

L4 ANSWER 7 OF 20 ZCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:580016 ZCAPLUS
DOCUMENT NUMBER: 139:292219
TITLE: Solid Phase Synthesis of 2-Aminoquinazoline-Based Compounds
AUTHOR(S): Srivastava, Gaurav K.; Kesarwani, Amit P.; Grover, Rajesh K.; Roy, Raja; Srinivasan, T.; Kundu, Bijoy
CORPORATE SOURCE: Medicinal Chemistry Division and NMR Lab, Sophisticated Analytical Instrumentation Facility, Central Drug Research Institute, Lucknow, IA, 226001,

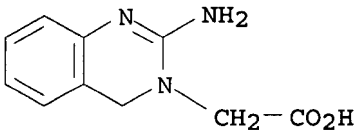
10/ 541,535

USA
SOURCE: Journal of Combinatorial Chemistry (2003), 5(6), 769-774
CODEN: JCCHFF; ISSN: 1520-4766
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 139:292219

AB A versatile method for the solid-phase synthesis of 2-aminoquinazoline-based derivs., 3-substituted-3,4-dihydroquinazolin-2-amines and imidazoquinazolines, has been developed. They were obtained by treating the amino group of polymer-linked amino acids with 2-nitrobenzaldehyde followed by reduction of the nitro group to an amine. Cyclization of the resulting immobilized intermediates with cyanogen bromide followed by acidic/basic cleavage yielded the desired quinazoline-based compds. in high yields and purities.

IT 603998-03-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(solid-phase synthesis of dihydroquinazolinamines and imidazoquinazolines by treating polymer-linked amino acids with nitrobenzaldehyde followed by reduction)

RN 603998-03-4 ZCAPLUS
CN 3(4H)-Quinazolineacetic acid, 2-amino-, monohydrobromide (9CI) (CA INDEX NAME)




● HBr

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 8 OF 20 ZCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:90046 ZCAPLUS
DOCUMENT NUMBER: 136:134782
TITLE: Preparation of anagrelide related compounds via nitration of dihalobenzaldehydes.
INVENTOR(S): Lang, Philip Charles; Spencer, Roxanne Paula; Yeh, Wen-Lung; Roth, Michael Joseph
PATENT ASSIGNEE(S): Shire US Inc., USA
SOURCE: PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2002008228 | A2 | 20020131 | WO 2001-GB3362 | 20010726 |
| WO 2002008228 | A3 | 20031009 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT,

RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

| | | | | |
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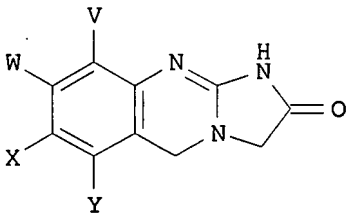
| US 6388073 | B1 | 20020514 | US 2000-625962 | 20000726 |
| CA 2417001 | A1 | 20020131 | CA 2001-2417001 | 20010726 |
| EP 1373268 | A2 | 20040102 | EP 2001-951826 | 20010726 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| EP 1700840 | A2 | 20060913 | EP 2006-13049 | 20010726 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| EP 1700841 | A2 | 20060913 | EP 2006-13050 | 20010726 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| EP 1700859 | A2 | 20060913 | EP 2006-13051 | 20010726 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| EP 1700842 | A2 | 20060913 | EP 2006-13052 | 20010726 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| EP 1700843 | A2 | 20060913 | EP 2006-13053 | 20010726 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| US 2003060630 | A1 | 20030327 | US 2002-134088 | 20020425 |
| US 6653500 | B2 | 20031125 | | |

PRIORITY APPLN. INFO.:

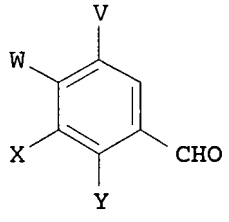
| | | |
|---|---|---|
| US 2000-625962 | A | 20000726 |
| EP 2001-951826 | A3 | 20010726 |
| WO 2001-GB3362 | W | 20010726 |

OTHER SOURCE(S): CASREACT 136:134782; MARPAT 136:134782

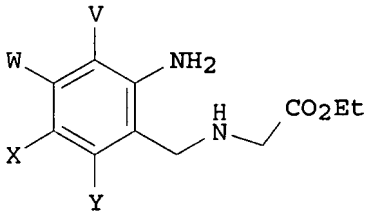
GI



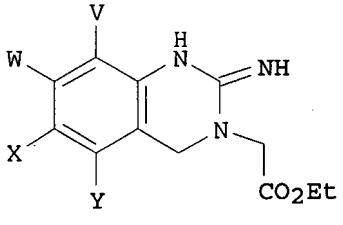
I



II



III



IV

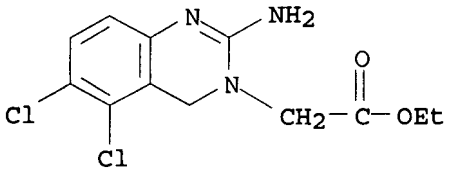
AB Title compds. (I; X, Y = F, Cl, Br, iodo; V, W = H, F, Cl, Br, iodo), were prepared in 7 steps from aldehydes (II; variables as above) via successive nitration, aldehyde reduction, chlorination, amination, and NO2 reduction to give (III; variables as above) followed by bromocyanation to give (IV; variables as above), and cyclization. Thus, Et N-(6-amino-2,3-

dichlorobenzyl)glycine (preparation given) was refluxed 1 h with CNBr in PhMe to give 96-98% Et 5,6-dichloro-3,4-dihydro-1(1H)-iminoquinazoline-3-acetate hydrobromide. The latter was stirred with Et3N in H2O for 2 h to give 86-88% 6,7-dichloro-1,5-dihydroimidazo[2,1-b]quinazolin-2(3H)-one.

IT 70381-75-8P
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of anagrelide related compds. via nitration of dihalobenzaldehydes)

RN 70381-75-8 ZCAPLUS

CN 3(4H)-Quinazolineacetic acid, 2-amino-5,6-dichloro-, ethyl ester, monohydrobromide (9CI) (CA INDEX NAME)



● HBr

L4 ANSWER 9 OF 20 ZCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1997:749954 ZCAPLUS

DOCUMENT NUMBER: 128:75359

TITLE: A convenient large-scale synthesis of ethyl (2-cyanimino-5,6-dichloro-1,2,3,4-tetrahydroquinazolin-3-yl)acetate

AUTHOR(S): Trinka, P.; Reiter, Jozsef

CORPORATE SOURCE: EGIS Pharmaceuticals Ltd., Budapest, H-1475, Hung.

SOURCE: Journal fuer Praktische Chemie/Chemiker-Zeitung (1997), 339(8), 750-753
CODEN: JPCCEM; ISSN: 0941-1216

PUBLISHER: Johann Ambrosius Barth

DOCUMENT TYPE: Journal

LANGUAGE: English

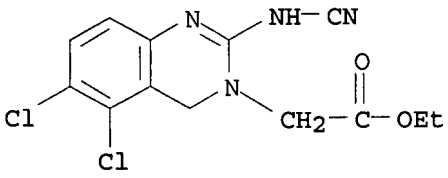
OTHER SOURCE(S): CASREACT 128:75359

AB Attempts to elaborate practical routes, applicable for industrial scale for the synthesis of the title compound as anagrelide precursor starting either from 2-amino-5,6-dichlorobenzylamine or N-(2-amino-5,6-dichlorobenzyl)glycinate are reported. The reaction of the latter compound with (PhO)2C:NCN in MeCN gave the desired product in 95% yield within 2 h.

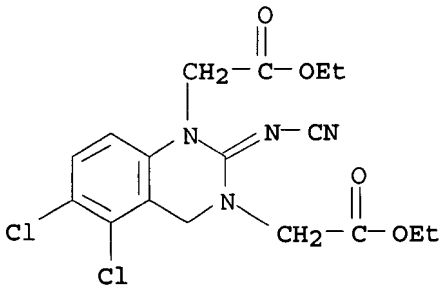
IT 146374-56-3P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(large-scale synthesis of anagrelide precursor [chloro(cyanimino)hydroquinazolinyl]acetate)

RN 146374-56-3 ZCAPLUS

CN 3(4H)-Quinazolineacetic acid, 5,6-dichloro-2-(cyanoamino)-, ethyl ester (9CI) (CA INDEX NAME)



IT 200571-16-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of anagrelide precursor [chloro(cyanimino)hydroquinazolinyl]acetate)
RN 200571-16-0 ZCAPLUS
CN 1,3(2H,4H)-Quinazolinediacetic acid, 5,6-dichloro-2-(cyanoimino)-, diethyl ester (9CI) (CA INDEX NAME)



L4 ANSWER 10 OF 20 ZCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1995:959882 ZCAPLUS
DOCUMENT NUMBER: 124:44698
TITLE: Isolation and identification of seven metabolites of a water-soluble platelet aggregation inhibitor in rat urine
AUTHOR(S): Tanaka, M.; Ishikawa, F.; Hakusui, H.
CORPORATE SOURCE: Drug Metabolism and Analytical Chemistry Research Center, Daiichi Pharmaceutical Co. Ltd., Tokyo, 134, Japan
SOURCE: Xenobiotica (1995), 25(11), 1247-57
CODEN: XENOBH; ISSN: 0049-8254
PUBLISHER: Taylor & Francis
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

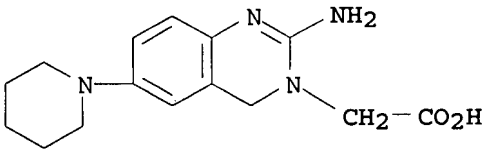
AB Seven metabolites of 7-piperidino-1,2,3,4,5-tetrahydroimidazo[2,1-b]quinazolin-2-one dihydrochloride monohydrate (DN-9693) were isolated from rat urine by extraction with Amberlite XAD-2 and purification by silica gel and Sephadex LH-20 open-column chromatog. and preparative high-performance liquid chromatog. (HPLC). The structure assignment of the metabolites was performed by field desorption mass spectrometry and 200-MHz Fourier transform NMR spectroscopic anal. and comparison with authentic stds. when available. DN-9693 underwent metabolism mainly at the piperidine ring to give the 4-hydroxypiperidine derivative (III) and 2-hydroxy-piperidine derivative,

which is further metabolized to lactam (II) or δ-aminovaleric acid (V). The acid side chain of V was shortened by β-oxidation to form the 3-aminopropionic acid derivative (VII). V and/or VII underwent oxidative dealkylation to give the 7-amino derivative, which was conjugated with acetic acid to form the 7-acetylamino derivative (IV). DN-9693 also underwent hydrolysis of its lactam moiety to give VI. The urinary excretion of III, V and VII was determined by liquid chromatog./electrochem. (LC/EC) and V proved to be the major metabolite in rat urine. A procedure is also presented for the identification of DN-9693 metabolites using LC/EC.

IT 172271-02-2
RL: ANT (Analyte); BSU (Biological study, unclassified); MFM (Metabolic formation); ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative)
(DN-9693 metabolite isolation and identification in rat urine)

RN 172271-02-2 ZCAPLUS

CN 3(4H)-Quinazolineacetic acid, 2-amino-6-(1-piperidinyl)- (9CI) (CA INDEX NAME)




L4 ANSWER 11 OF 20 ZCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1995:528642 ZCAPLUS

DOCUMENT NUMBER: 122:265395

TITLE: Process for the preparation of 6,7-dichloro-1,5-dihydroimidazo[2,1-b]quinazolin-2(3H)-one

INVENTOR(S): Reiter, Jozsef; Trinka, Peter; Toempe, Peter; Szabo, Eva; Slegel, Peter; Brlik, Janos; Halbauer, Nee Nagy Agnes; Sztruhar, Ilona; Kenyeres, Nee Feher Magdolna; et al.

PATENT ASSIGNEE(S): EGIS Gyogyszergyar, Hung.

SOURCE: U.S., 7 pp. Cont.-in-part of U.S. Ser. No. 886,605, abandoned.
CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

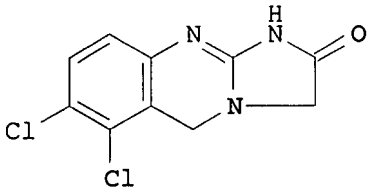
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 5391737 | A | 19950221 | US 1993-156974 | 19931124 |
| HU 61003 | A2 | 19921130 | HU 1991-1707 | 19910522 |
| HU 208681 | B | 19931228 | | |
| HU 62586 | A2 | 19930528 | HU 1991-1708 | 19910522 |
| HU 209633 | B | 19940928 | | |

PRIORITY APPLN. INFO.:

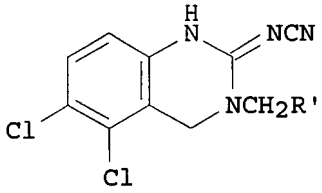
| | | |
|---|---|---|
| HU 1991-1707 | A | 19910522 |
| HU 1991-1708 | A | 19910522 |
| US 1992-886605 | B2 | 19920521 |

OTHER SOURCE(S): CASREACT 122:265395; MARPAT 122:265395

GI



I



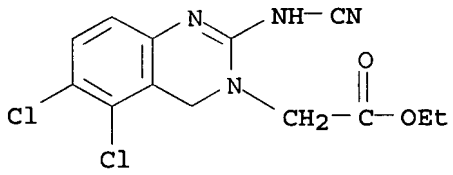
II

AB This invention relates to a new and improved process for the preparation of 6,7-dichloro-1,5-dihydroimidazo[2,1-b]quinazolin-2(3H)-one (I, anagrelide), a valuable blood platelet antiaggregative compound According to the process of the invention, I is prepared by subjecting a new 2-cyanoiminoquinazoline derivative of the general formula II wherein R' stands for cyano or a group of the formula COOR1, in the latter R1 representing lower alkyl optionally carrying a Ph substituent, to thermal cyclization in an acidic medium. The invention also relates to new 2-cyanoiminoquinazolines of the general formula II used for the production of anagrelide and to the preparation of the said compds. The invention provides an advantageous process for the preparation of anagrelide which is devoid of the drawbacks of the hitherto known processes and renders possible the production of the compound of the formula I on an industrial scale. Thus, e.g.,
thermal cyclization of Et (2-cyanoimino-5,6-dichloro-1,2,3,4-tetrahydroquinazolin-3-yl)acetate (preparation given) in ethylene glycol/HCl at 115° afforded 93.0% 6,7-dichloro-1,5-dihydroimidazo[2,1-b]quinazolin-2[3H]-one base.

IT 146374-56-3P, Ethyl (2-cyanoimino-5,6-dichloro-1,2,3,4-tetrahydroquinazolin-3-yl)acetate 146374-59-6P, Benzyl (2-cyanoimino-5,6-dichloro-1,2,3,4-tetrahydroquinazolin-3-yl)acetate
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of anagrelide via thermal cyclization of 2-cyanoiminoquinazoline derivs.)

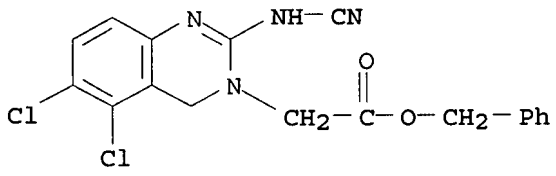
RN 146374-56-3 ZCAPLUS

CN 3(4H)-Quinazolineacetic acid, 5,6-dichloro-2-(cyanoamino)-, ethyl ester (9CI) (CA INDEX NAME)



RN 146374-59-6 ZCAPLUS

CN 3(4H)-Quinazolineacetic acid, 5,6-dichloro-2-(cyanoamino)-, phenylmethyl ester (9CI) (CA INDEX NAME)

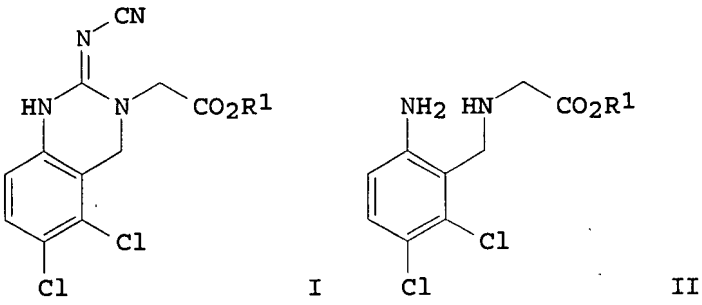


10/ 541,535

L4 ANSWER 12 OF 20 ZCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1994:270448 ZCAPLUS
DOCUMENT NUMBER: 120:270448
TITLE: Process for producing quinazolineacetic acid esters via cyclization of N-cyanimidodithiocarbonates with aminobenzylglycinates catalyzed by mercury or lead compounds
INVENTOR(S): Trinka, Peter; Reiter, Jozsef; Pongo, Laszlo
PATENT ASSIGNEE(S): EGIS Gyogyszergyar RT., Hung.
SOURCE: Hung. Teljes, 16 pp.
CODEN: HUXXBU
DOCUMENT TYPE: Patent
LANGUAGE: Hungarian
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| HU 64045 | A2 | 19931129 | HU 1992-1223 | 19920410 |
| HU 213619 | B | 19970828 | | |
| PRIORITY APPLN. INFO.: | | | HU 1992-1223 | 19920410 |

OTHER SOURCE(S): CASREACT 120:270448; MARPAT 120:270448
GI

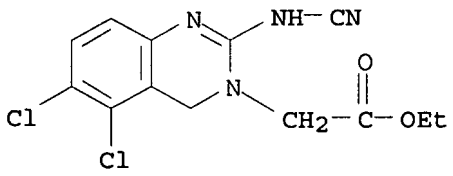



I II

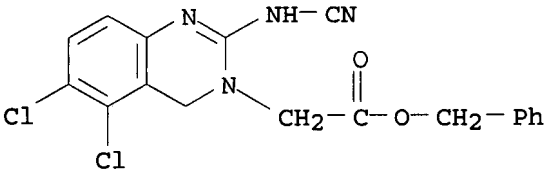
AB Title compds. I (R1 = C1-4 alkyl which may contain a Ph group) were prepared by cyclization of diamino esters II (R1 as above) with cyanimide derivs. (R2S)2C:NCN (R2 = C1-4 alkyl which may contain a Ph group) in presence of a catalyst. Thus, reaction of (MeS)2C:NCN with II (R1 = Et) in presence of Hg(II) oxide afforded 81.5% I (R1 = Et).

IT 146374-56-3P 146374-59-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 146374-56-3 ZCAPLUS
CN 3(4H)-Quinazolineacetic acid, 5,6-dichloro-2-(cyanoamino)-, ethyl ester (9CI) (CA INDEX NAME)



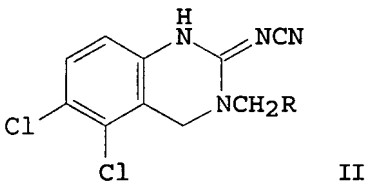

RN 146374-59-6 ZCAPLUS
CN 3(4H)-Quinazolineacetic acid, 5,6-dichloro-2-(cyanoamino)-, phenylmethyl ester (9CI) (CA INDEX NAME)



L4 ANSWER 13 OF 20 ZCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1993:191755 ZCAPLUS
DOCUMENT NUMBER: 118:191755
TITLE: Preparation of anagrelide
INVENTOR(S): Reiter, Jozef; Trinka, Peter; Tompe, Peter; Szabo, Eva; Slegel, Peter; Brlik, Janos; Halbauer, Agnes; Sztruhar, Ilona; Kenyeres, Magdolna; et al.
PATENT ASSIGNEE(S): Egis Gyogyszergyar, Hung.
SOURCE: Eur. Pat. Appl., 21 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | | DATE |
|---|---|---|---|---|---|
| EP 514917 | A1 | 19921125 | EP 1992-108656 | | 19920522 |
| EP 514917 | B1 | 19961227 | | | |
| R: AT, BE, CH, DE, DK, ES, FR, GR, IT, LI, NL, SE | | | | | |
| HU 61003 | A2 | 19921130 | HU 1991-1707 | | 19910522 |
| HU 208681 | B | 19931228 | | | |
| HU 62586 | A2 | 19930528 | HU 1991-1708 | | 19910522 |
| HU 209633 | B | 19940928 | | | |
| JP 05271200 | A | 19931019 | JP 1992-151259 | | 19920520 |
| GB 2256195 | A | 19921202 | GB 1992-10908 | | 19920521 |
| GB 2256195 | B | 19941221 | | | |
| RU 2042678 | C1 | 19950827 | RU 1992-5011723 | | 19920521 |
| CZ 281671 | B6 | 19961211 | CZ 1992-1538 | | 19920522 |
| AT 146789 | T | 19970115 | AT 1992-108656 | | 19920522 |
| ES 2095349 | T3 | 19970216 | ES 1992-108656 | | 19920522 |
| PRIORITY APPLN. INFO.: | | | HU 1991-1707 | A | 19910522 |
| | | | HU 1991-1708 | A | 19910522 |

OTHER SOURCE(S): CASREACT 118:191755; MARPAT 118:191755
GI

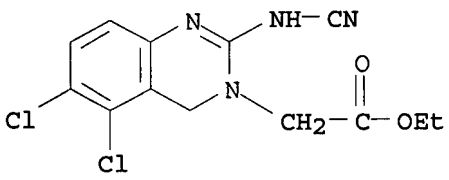


II

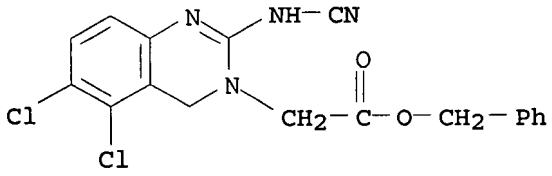
AB The title compound (I) was prepared by cyclization of cyanoiminotetrahydroquinazolinylacetates II [R = cyano, (ar)alkoxycarbonyl]. Thus, Et (2-amino-5,6-dichlorobenzylamino)acetate was cyclocondensed with (PhO)2C:NCN to give 77.6% II (R = CO2Et) which was stirred 30 min at 115° with HCl in HOCH2CH2OH to give 82.9% I.

10/ 541,535

IT 146374-56-3P 146374-59-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and cyclization of, in preparation of anagrelide)
RN 146374-56-3 ZCAPLUS
CN 3(4H)-Quinazolineacetic acid, 5,6-dichloro-2-(cyanoamino)-, ethyl ester (9CI) (CA INDEX NAME)



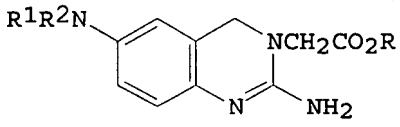
RN 146374-59-6 ZCAPLUS
CN 3(4H)-Quinazolineacetic acid, 5,6-dichloro-2-(cyanoamino)-, phenylmethyl ester (9CI) (CA INDEX NAME)



L4 ANSWER 14 OF 20 ZCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1989:23910 ZCAPLUS
DOCUMENT NUMBER: 110:23910
TITLE: Quinazolineacetic acid derivatives as platelet aggregation inhibitors
INVENTOR(S): Ishikawa, Fumyoshi; Ono, Kenji
PATENT ASSIGNEE(S): Daiichi Seiyaku Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 6 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| JP 63196573 | A | 19880815 | JP 1987-29236 | 19870210 |
| JP 07030046 | B | 19950405 | | |
| PRIORITY APPLN. INFO.: | | | JP 1987-29236 | 19870210 |

OTHER SOURCE(S): MARPAT 110:23910
GI



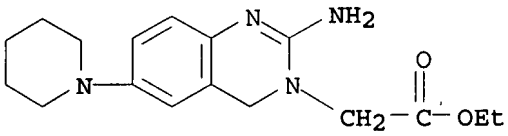
I

AB The title derivs. I (R = H, alkyl; R1, R2 = alkyl, R1R2 = alkylene) and

their acid salts are prepared as platelet aggregation inhibitors. Reaction of 4.0 g 2-nitro-5-chlorobenzoic acid with 8.5 g piperidine gave 3.5 g 2-nitro-5-(1-piperidinyl)benzoic acid, which was reduced by NaBH4 in THF to give 2.7 g 2-nitro-5-(1-piperidinyl)benzyl alc. (II). II (1.08 g) was chlorinated by SOCl2, then treated with 3.2 g glycine Et ester-HCl in EtOH containing Et3N to give 0.65 g Et 2-nitro-5-(1-piperidinyl)benzylaminoacetate (III). A solution of 0.65 g III in EtOH was hydrogenated over PtO2 and the product was treated with 0.22 g BrCN in EtOH at room temperature overnight and then with HCl to give 0.44 g I.HBr.HCl.H2O [R = Et, R1R2 = (CH2)5], which showed IC50 of 25 μM against collagen-induced aggregation.

IT 118159-36-7P 118159-37-8P 118159-38-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as platelet aggregation inhibitor)

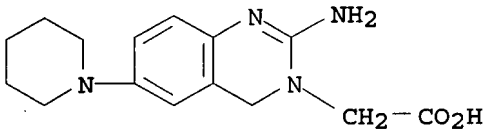
RN 118159-36-7 ZCAPLUS
CN 3(4H)-Quinazolineacetic acid, 2-amino-6-(1-piperidinyl)-, ethyl ester, hydrobromide hydrochloride (9CI) (CA INDEX NAME)



●x HBr

●x HCl

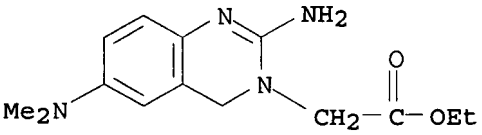
RN 118159-37-8 ZCAPLUS
CN 3(4H)-Quinazolineacetic acid, 2-amino-6-(1-piperidinyl)-, hydrobromide hydrochloride (9CI) (CA INDEX NAME)



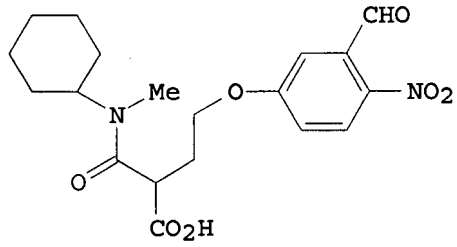
●x HBr

●x HCl

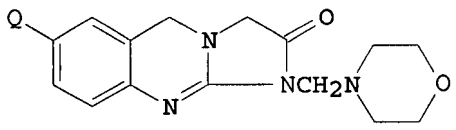
RN 118159-38-9 ZCAPLUS
CN 3(4H)-Quinazolineacetic acid, 2-amino-6-(dimethylamino)-, ethyl ester (9CI) (CA INDEX NAME)



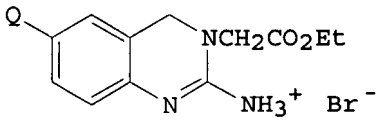
L4 ANSWER 15 OF 20 ZCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1988:570369 ZCAPLUS
DOCUMENT NUMBER: 109:170369
TITLE: Inhibitors of cyclic AMP phosphodiesterase. 4. Synthesis and evaluation of potential prodrugs of lixazinone (N-cyclohexyl-N-methyl-4-[(1,2,3,5-tetrahydro-2-oxoimidazo[2,1-b]quinazolin-7-yl)oxy]butyramide, RS-82856)
AUTHOR(S): Venuti, Michael C.; Alvarez, Robert; Bruno, John J.; Strosberg, Arthur M.; Gu, Leo; Chiang, Hi Shi; Massey, Ian J.; Chu, Nancy; Fried, John H.
CORPORATE SOURCE: Inst. Bio-Organic Chem., Syntex Research, Palo Alto, CA, 94304, USA
SOURCE: Journal of Medicinal Chemistry (1988), 31(11), 2145-52
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 109:170369
GI



II

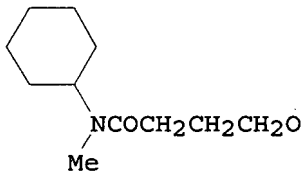


III



IV

Q=

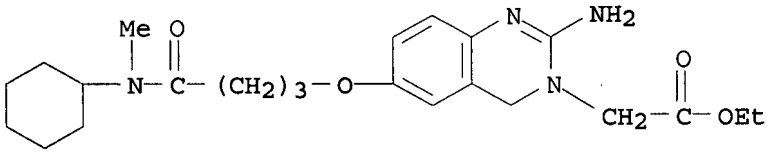


AB The cyclic AMP phosphodiesterase (cAMP PDE) inhibitor and cardiotonic agent lixazinone [N-cyclohexyl-N-methyl-4-[(1,2,3,5-tetrahydro-2-oxoimidazo[2,1-b]quinazolin-7-yl)oxy]butyramide, RS-82856, I] and its acid and base addition salts were found to be insufficiently soluble in formulations suitable for i.v. administration. Potential prodrugs with enhanced aqueous solubility were designed to deliver I by three distinct mechanisms: (1) decarboxylation of α-carboxamides; (2) hydrolytic loss of a solubilizing N-1 (acyloxy)methyl or (N,N-dialkylamino)methyl moiety; or

(3) intramol. closure of a guanidino ester or amide. The target compds. were evaluated as deliver systems for I by three criteria: (1) chemical conversion rate to I under physiol. conditions; (2) inhibition of type IV cAMP PDE at a fixed time point; and (3) in vivo inotropic activity in anesthetized dogs by both i.v. and oral administration. Release of I from α-carboxamide II was too slow to be of value as a prodrug of I, since decarboxylation could be induced only by strong acid, conditions under which hydrolytic ring opening severely competed. Conversely, I was released too readily on exposure of (N,N,-dialkylamino)methyl derivs., e.g. III, to physiol. conditions, although no large increase in aqueous solubility was realized. Both the physicochem. and in vitro studies indicated that ring closure of the guanidinium esters and amides, e.g. II, to I was quant. and pH- and time-dependent, suggesting the possibility of delivery of the open, water-soluble prodrug form, followed by closure to I in plasma. Detailed examination of these agents in vivo, demonstrated that only those compds. that rapidly cyclized to I, as measured by plasma levels of I exhibited inotropic activity, indicating that the open prodrug form was not efficiently absorbed upon oral administration.

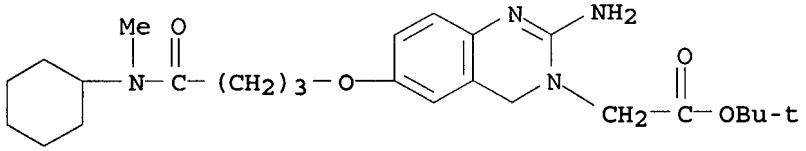
IT 114703-76-3P 114703-82-1P 114703-83-2P
114703-84-3P 114703-85-4P 114703-86-5P
115623-42-2P 116005-78-8P 116005-82-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and biol. evaluation of, as lixazinone prodrug)

RN 114703-76-3 ZCAPLUS
CN 3(4H)-Quinazolineacetic acid, 2-amino-6-[4-(cyclohexylmethylamino)-4-oxobutoxy]-, ethyl ester, monohydrobromide (9CI) (CA INDEX NAME)



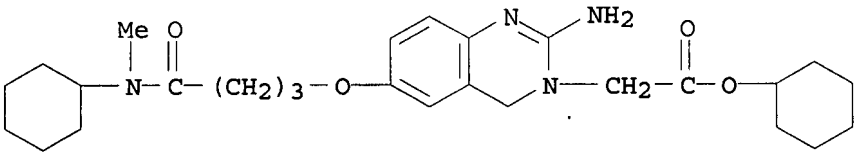
● HBr

RN 114703-82-1 ZCAPLUS
CN 3(4H)-Quinazolineacetic acid, 2-amino-6-[4-(cyclohexylmethylamino)-4-oxobutoxy]-, 1,1-dimethylethyl ester, monohydrobromide (9CI) (CA INDEX NAME)



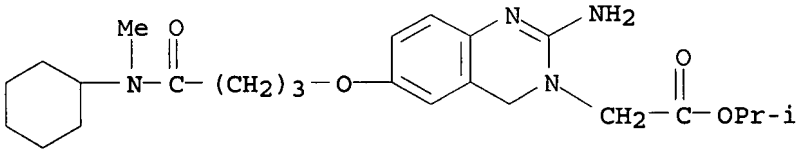
● HBr

RN 114703-83-2 ZCAPLUS
CN 3(4H)-Quinazolineacetic acid, 2-amino-6-[4-(cyclohexylmethylamino)-4-oxobutoxy]-, cyclohexyl ester, monohydrobromide (9CI) (CA INDEX NAME)



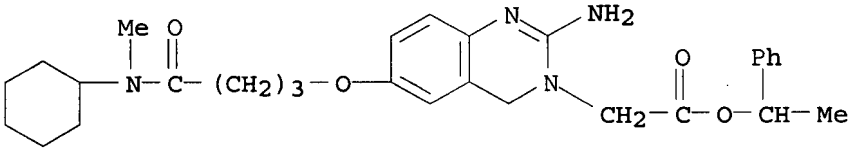
● HBr

RN 114703-84-3 ZCAPLUS
CN 3(4H)-Quinazolineacetic acid, 2-amino-6-[4-(cyclohexylmethylamino)-4-oxobutoxy]-, 1-methylethyl ester, monohydrobromide (9CI) (CA INDEX NAME)



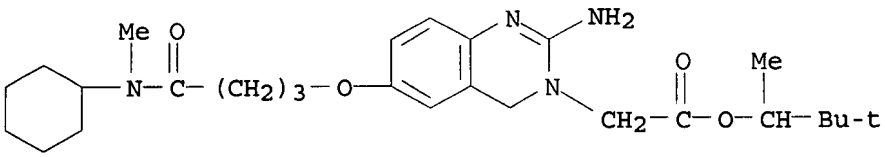
● HBr

RN 114703-85-4 ZCAPLUS
CN 3(4H)-Quinazolineacetic acid, 2-amino-6-[4-(cyclohexylmethylamino)-4-oxobutoxy]-, 1-phenylethyl ester, monohydrobromide (9CI) (CA INDEX NAME)



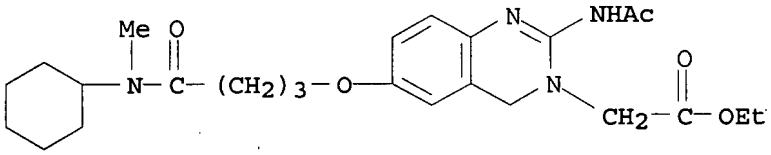
● HBr

RN 114703-86-5 ZCAPLUS
CN 3(4H)-Quinazolineacetic acid, 2-amino-6-[4-(cyclohexylmethylamino)-4-oxobutoxy]-, 1,2,2-trimethylpropyl ester, monohydrobromide (9CI) (CA INDEX NAME)

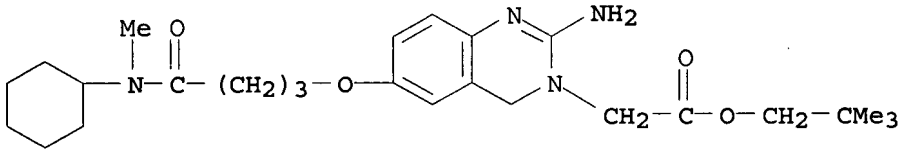


● HBr

RN 115623-42-2 ZCAPLUS
CN 3(4H)-Quinazolineacetic acid, 2-(acetylamino)-6-[4-(cyclohexylmethylamino)-4-oxobutoxy]-, ethyl ester (9CI) (CA INDEX NAME)

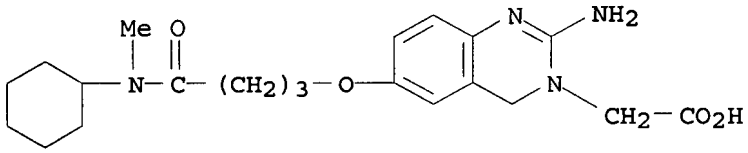


RN 116005-78-8 ZCAPLUS
CN 3(4H)-Quinazolineacetic acid, 2-amino-6-[4-(cyclohexylmethylamino)-4-oxobutoxy]-, 2,2-dimethylpropyl ester, monohydrobromide (9CI) (CA INDEX NAME)



● HBr

RN 116005-82-4 ZCAPLUS
CN 3(4H)-Quinazolineacetic acid, 2-amino-6-[4-(cyclohexylmethylamino)-4-oxobutoxy]-, dihydrobromide (9CI) (CA INDEX NAME)

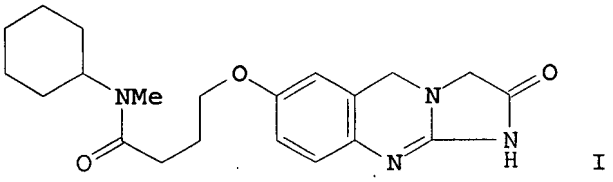


●2 HBr

L4 ANSWER 16 OF 20 ZCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1988:534889 ZCAPLUS

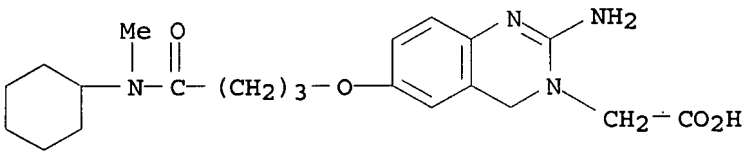
10/ 541,535

DOCUMENT NUMBER: 109:134889
TITLE: Parenteral formulation development for the positive inotropic agent RS-82856. Hydrolysis and oxidation kinetics, solubility and i.v. formulation considerations
AUTHOR(S): Gu, Leo; Oanh Huynh; Strickley, Robert G.; Lin, Li Hwa; Visor, Gary C.
CORPORATE SOURCE: Inst. Pharm. Sci., Syntex Res., Palo Alto, CA, USA
SOURCE: International Journal of Pharmaceutics (1988), 45(1-2), 129-38
CODEN: IJPHDE; ISSN: 0378-5173
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB The degradation kinetics and solubility of RS-82856 hydrogen sulfate (I hydrogen sulfate) in aqueous and organic solns. were investigated. I reached a .apprx.50/50 equilibrium in water with its imidazole-ring-opened product (RS-31621), which then further degraded to give several secondary products. The rate consts. for the acid catalyzed (kH), spontaneous or water-catalyzed (k0) and base-catalyzed (kOH) reactions for both the forward and reverse reactions were determined at 40, 60 and 80°. The reacting species responsible for each reaction were proposed. Biphasic kinetics were also observed for the autoxidn. of I hydrogen sulfate in organic solvents; the 5-oxo analog (RS-82890) was the only product detected. The t90s in propylene glycol, dimethylacetamide and DMSO for the hydrogen sulfate salt at 25° are <4 wk. These stability results and various solubility data were combined to evaluate possible i.v. formulations for toxicol. and clin. studies. All solution formulations (aqueous, aqueous-organic or organic) are unsuitable for I hydrogen sulfate and alternatives should be sought.
IT 114703-77-4
RL: FORM (Formation, nonpreparative)
(formation of, as RS-82856 degradation product, parenteral formulation in relation to)
RN 114703-77-4 ZCAPLUS
CN 3(4H)-Quinazolineacetic acid, 2-amino-6-[4-(cyclohexylmethylamino)-4-oxobutoxy]- (9CI) (CA INDEX NAME)



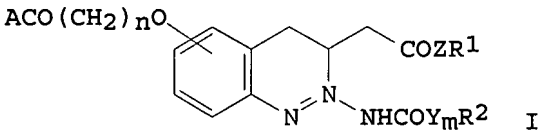

L4 ANSWER 17 OF 20 ZCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1988:493050 ZCAPLUS
DOCUMENT NUMBER: 109:93050

10/ 541,535

TITLE: Preparation and testing of dihydroquinazolinyloxyalkylamides as cardiotonics and antithrombotics
INVENTOR(S): Venuti, Michael C.
PATENT ASSIGNEE(S): Syntex (U.S.A.), Inc., USA
SOURCE: U.S., 23 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 4739056 | A | 19880419 | US 1986-935659 | 19861126 |
| PRIORITY APPLN. INFO.: | | | US 1986-935659 | 19861126 |

OTHER SOURCE(S): MARPAT 109:93050
GI

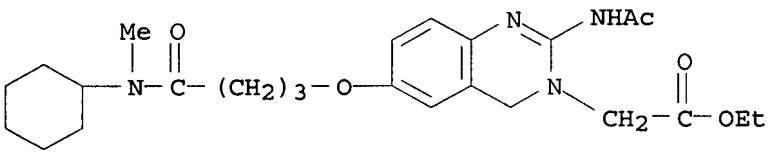


I

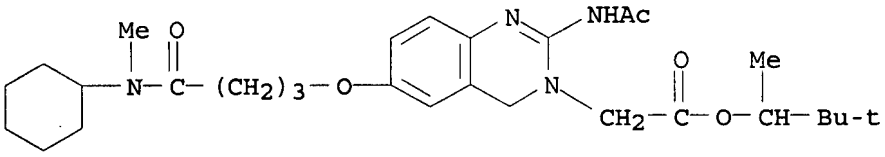
AB The title compds. [I; R1-R4 = H, alkyl optionally substituted by Cl3C or F3C, (substituted) cycloalkyl, cycloalkylalkyl, Ph, phenylalkyl; R2R4, R1R3 = atoms to complete heterocyclic rings; A = amino; Y = O, NR4; Z = O, NR3; m = 0,1; n = 1-6] were prepared as antithrombotics and inotropics. Glycine tert-Bu ester-HCl was stirred overnight with NaOAc in EtOH and the filtered mixture was treated with N-cyclohexyl-N-methyl-4-(3-formyl-4-nitrophenyl)oxybutyramide and then NaBH3CN to give N-cyclohexyl-N-methyl-4-[2-amino-3-(tert-butyloxycarbonylmethyl)-3,4-dihydroquinazolin-6-yl]oxybutyramide-HBr. The latter was acetylated with Ac2O/Et3N in CH2Cl2 followed by stirring overnight with HBr/HOAc in EtOAc/EtOH to give N-cyclohexyl-N methyl-4-[2-acetamido-3-(ethoxycarbonylmethyl)-3,4-dihydroquinazolin-6-yl]oxybutyramide. The latter at 3.2 mg/kg intraduodenally in dogs increased right ventricular contractile force to 58% of the maximum value seen with isoproterenol.

IT 115623-42-2P 115623-43-3P 115623-44-4P
115623-45-5P 115623-46-6P 115623-47-7P
115623-48-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as cardiotonic and antithrombotic)

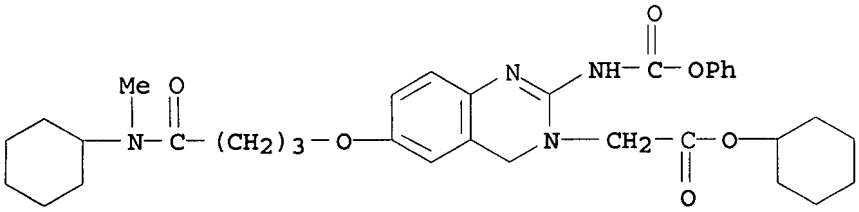
RN 115623-42-2 ZCAPLUS
CN 3(4H)-Quinazolineacetic acid, 2-(acetylamino)-6-[4-(cyclohexylmethylamino)-4-oxobutoxy]-, ethyl ester (9CI) (CA INDEX NAME)



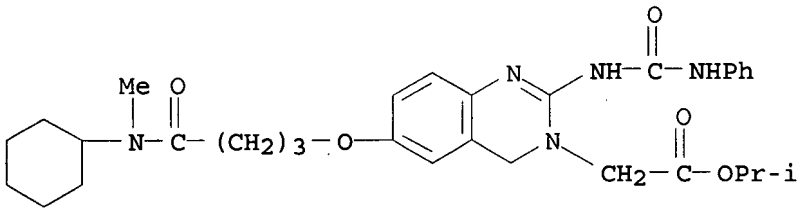

RN 115623-43-3 ZCAPLUS
CN 3(4H)-Quinazolineacetic acid, 2-(acetylamino)-6-[4-(cyclohexylmethylamino)-4-oxobutoxy]-, 1,2,2-trimethylpropyl ester (9CI) (CA INDEX NAME)



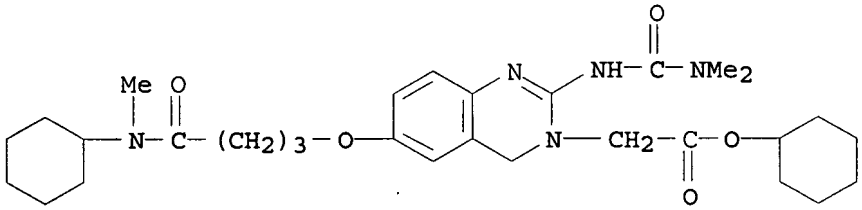
RN 115623-44-4 ZCAPLUS
CN 3(4H)-Quinazolineacetic acid, 6-[4-(cyclohexylmethylamino)-4-oxobutoxy]-2-[(phenoxycarbonyl)amino]-, cyclohexyl ester (9CI) (CA INDEX NAME)



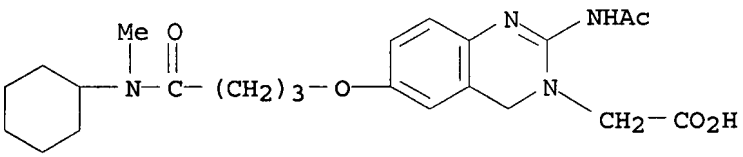
RN 115623-45-5 ZCAPLUS
CN 3(4H)-Quinazolineacetic acid, 6-[4-(cyclohexylmethylamino)-4-oxobutoxy]-2-[[(phenylamino)carbonyl]amino]-, 1-methylethyl ester (9CI) (CA INDEX NAME)



RN 115623-46-6 ZCAPLUS
CN 3(4H)-Quinazolineacetic acid, 6-[4-(cyclohexylmethylamino)-4-oxobutoxy]-2-[[(dimethylamino)carbonyl]amino]-, cyclohexyl ester (9CI) (CA INDEX NAME)

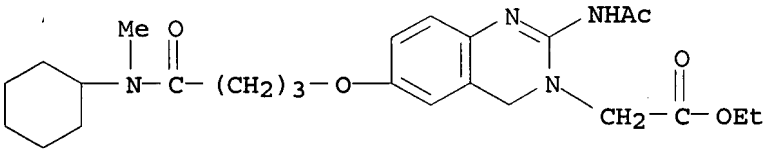


RN 115623-47-7 ZCAPLUS
CN 3(4H)-Quinazolineacetic acid, 2-(acetylamino)-6-[4-(cyclohexylmethylamino)-4-oxobutoxy]-, monohydrochloride (9CI) (CA INDEX NAME)



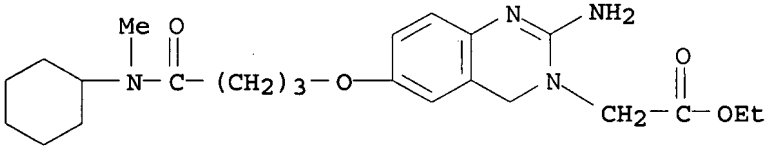
● HCl

RN 115623-48-8 ZCAPLUS
CN 3(4H)-Quinazolineacetic acid, 2-(acetylamino)-6-[4-(cyclohexylmethylamino)-4-oxobutoxy]-, ethyl ester, monohydrochloride (9CI) (CA INDEX NAME)



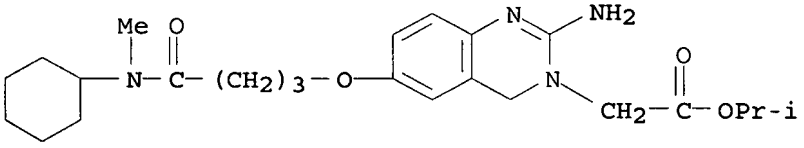
● HCl

IT 114703-76-3P 115623-49-9P 115623-50-2P
115653-85-5P 115653-86-6P 115653-87-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as intermediate for quinazoline cardiotonic)
RN 114703-76-3 ZCAPLUS
CN 3(4H)-Quinazolineacetic acid, 2-amino-6-[4-(cyclohexylmethylamino)-4-oxobutoxy]-, ethyl ester, monohydrobromide (9CI) (CA INDEX NAME)



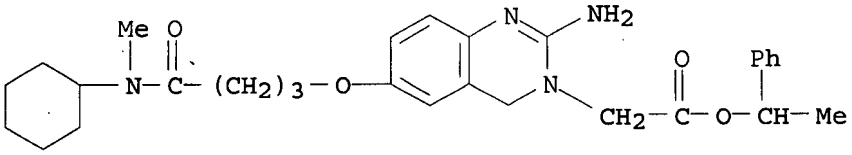
● HBr

RN 115623-49-9 ZCAPLUS
CN 3(4H)-Quinazolineacetic acid, 2-amino-6-[4-(cyclohexylmethylamino)-4-oxobutoxy]-, 1-methylethyl ester (9CI) (CA INDEX NAME)

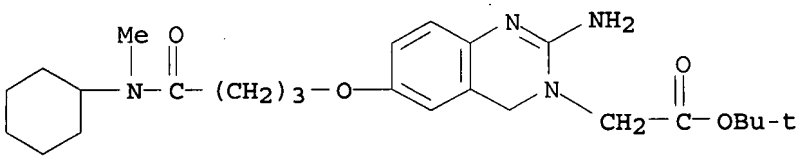


10/ 541,535

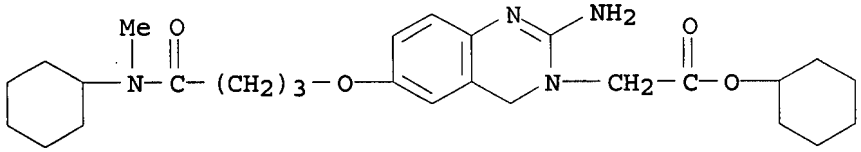
RN 115623-50-2 ZCAPLUS
CN 3(4H)-Quinazolineacetic acid, 2-amino-6-[4-(cyclohexylmethylamino)-4-oxobutoxy]-, 1-phenylethyl ester (9CI) (CA INDEX NAME)



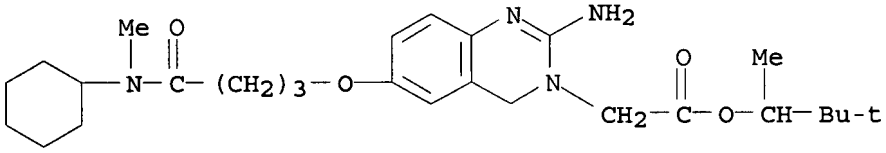
RN 115653-85-5 ZCAPLUS
CN 3(4H)-Quinazolineacetic acid, 2-amino-6-[4-(cyclohexylmethylamino)-4-oxobutoxy]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 115653-86-6 ZCAPLUS
CN 3(4H)-Quinazolineacetic acid, 2-amino-6-[4-(cyclohexylmethylamino)-4-oxobutoxy]-, cyclohexyl ester (9CI) (CA INDEX NAME)



RN 115653-87-7 ZCAPLUS
CN 3(4H)-Quinazolineacetic acid, 2-amino-6-[4-(cyclohexylmethylamino)-4-oxobutoxy]-, 1,2,2-trimethylpropyl ester (9CI) (CA INDEX NAME)



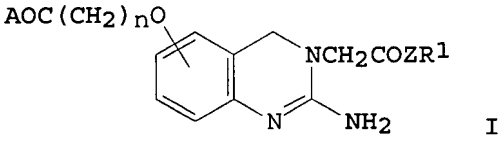
L4 ANSWER 18 OF 20 ZCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1988:406541 ZCAPLUS
DOCUMENT NUMBER: 109:6541
TITLE: Preparation, testing, and formulation of [2-amino-3-(acylmethyl)-3,4-dihydroquinazolinyloxy]alkanamides as cardiovascular agents
INVENTOR(S): Fried, John H.; Venuti, Michael C.
PATENT ASSIGNEE(S): Syntex (U.S.A.), Inc., USA
SOURCE: Eur. Pat. Appl., 27 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

10/ 541,535

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| EP 254327 | A2 | 19880127 | EP 1987-110796 | 19870724 |
| EP 254327 | A3 | 19891108 | | |
| R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE | | | | |
| US 4761416 | A | 19880802 | US 1986-889641 | 19860725 |
| DK 8703888 | A | 19880126 | DK 1987-3888 | 19870724 |
| AU 8776100 | A | 19880128 | AU 1987-76100 | 19870724 |
| JP 63039866 | A | 19880220 | JP 1987-186503 | 19870724 |
| ZA 8705469 | A | 19890329 | ZA 1987-5469 | 19870724 |
| PRIORITY APPLN. INFO.: | | | US 1986-889641 A | 19860725 |
| OTHER SOURCE(S): | CASREACT 109:6541; MARPAT 109:6541 | | | |

GI



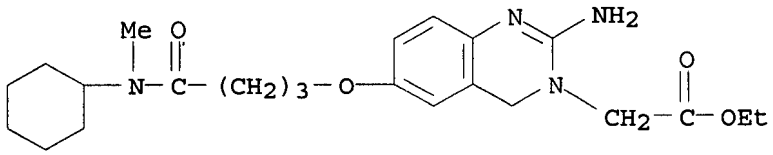

I

AB The title compds. (I; R1 = H, OH, Me, Et, cycloalkyl, hydroxyalkyl, alkoxy, halo, amino, etc.; A = amino; Z = O, NR2; R2 = R1; n = 1-6) and their pharmaceutically acceptable salts were prepared as cardiovascular agents. N-Cyclohexyl-N-methyl-4-(3-formyl-4-nitrophenoxy)butyramide and then NaBH3CN were added to a mixture of glycine Et ester-HCl and NaOAc in EtOH and the mixture was stirred 3 h. The residue was hydrogenated in EtOH over Pd/C and treated with BrCN to give N-cyclohexyl-N-methyl-4-[[2-amino-3-(ethoxycarbonylmethyl)-3,4-dihydroquinazolin-6-yl]oxy]butyramide. The latter inhibited human cAMP phosphodiesterase with an IC50 of 9.3 nM, and increased contractility of the right ventricle of dogs by 38-62% of the maximum values seen with isoproterenol.

IT 114703-76-3P 114703-77-4P 114703-82-1P
114703-83-2P 114703-84-3P 114703-85-4P
114703-86-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of, as cardiovascular agent)

RN 114703-76-3 ZCAPLUS

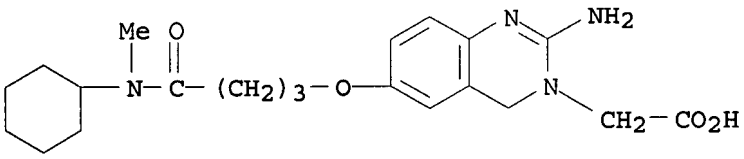
CN 3(4H)-Quinazolineacetic acid, 2-amino-6-[4-(cyclohexylmethylamino)-4-oxobutoxy]-, ethyl ester, monohydrobromide (9CI) (CA INDEX NAME)



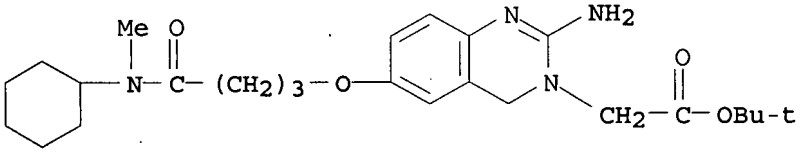

● HBr

RN 114703-77-4 ZCAPLUS

CN 3(4H)-Quinazolineacetic acid, 2-amino-6-[4-(cyclohexylmethylamino)-4-oxobutoxy]- (9CI) (CA INDEX NAME)

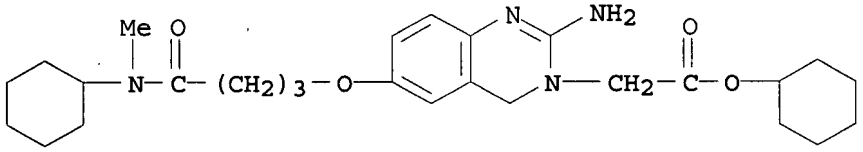


RN 114703-82-1 ZCAPLUS
CN 3(4H)-Quinazolineacetic acid, 2-amino-6-[4-(cyclohexylmethylamino)-4-oxobutoxy]-, 1,1-dimethylethyl ester, monohydrobromide (9CI) (CA INDEX NAME)



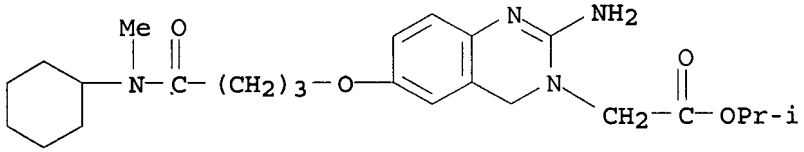
● HBr

RN 114703-83-2 ZCAPLUS
CN 3(4H)-Quinazolineacetic acid, 2-amino-6-[4-(cyclohexylmethylamino)-4-oxobutoxy]-, cyclohexyl ester, monohydrobromide (9CI) (CA INDEX NAME)



● HBr

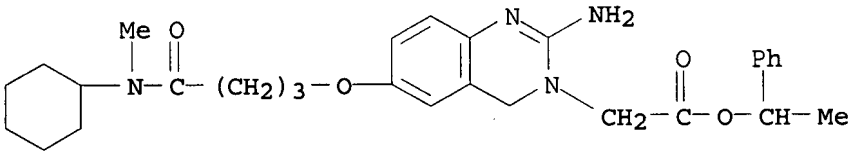
RN 114703-84-3 ZCAPLUS
CN 3(4H)-Quinazolineacetic acid, 2-amino-6-[4-(cyclohexylmethylamino)-4-oxobutoxy]-, 1-methylethyl ester, monohydrobromide (9CI) (CA INDEX NAME)



● HBr

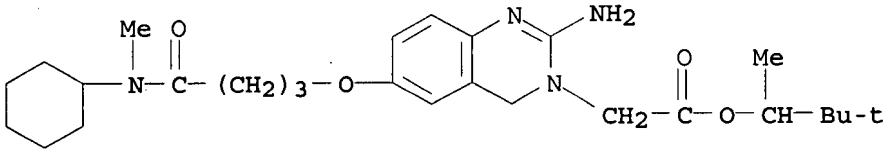
RN 114703-85-4 ZCAPLUS
CN 3(4H)-Quinazolineacetic acid, 2-amino-6-[4-(cyclohexylmethylamino)-4-

oxobutoxy]-, 1-phenylethyl ester, monohydrobromide (9CI) (CA INDEX NAME)



● HBr

RN 114703-86-5 ZCAPLUS
CN 3(4H)-Quinazolineacetic acid, 2-amino-6-[4-(cyclohexylmethylamino)-4-oxobutoxy]-, 1,2,2-trimethylpropyl ester, monohydrobromide (9CI) (CA INDEX NAME)

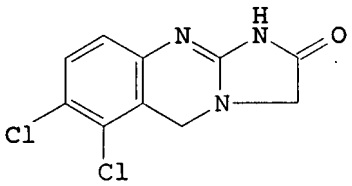


● HBr

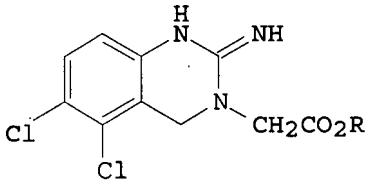
L4 ANSWER 19 OF 20 ZCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1983:179403 ZCAPLUS
DOCUMENT NUMBER: 98:179403
TITLE: 6,7-Dichloro-1,5-dihydroimidazo[2,1-b]quinazolin-2(3H)-one
INVENTOR(S): Jenks, Thomas A.; Beverung, Warren N., Jr.; Partyka, Richard A.
PATENT ASSIGNEE(S): Bristol-Myers Co. , USA
SOURCE: Can., 25 pp. Division of Can. Appl. No. 324,838.
CODEN: CAXXA4
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| CA 1137474 | A2 | 19821214 | CA 1981-381570 | 19810710 |
| US 4146718 | A | 19790327 | US 1978-894464 | 19780410 |
| CA 1109067 | A1 | 19810915 | CA 1979-324838 | 19790403 |
| PRIORITY APPLN. INFO.: | | | US 1978-894464 A | 19780410 |
| | | | CA 1979-324838 A3 | 19790403 |

GI



I



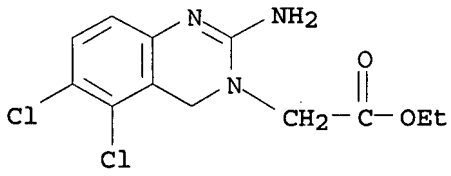
II

AB Title compound (I) was prepared by cyclization of II.HX (R = alkyl; X = Cl, Br, iodo) in presence of a base. Thus, II.HBr (R = Et) was prepared in 6 steps from 1,2,3-Cl3C6H3, and was cyclized in the presence of 1 mol NEt3 in EtOH to give 92% I.

IT 70381-75-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and cyclization of)

RN 70381-75-8 ZCAPLUS

CN 3(4H)-Quinazolineacetic acid, 2-amino-5,6-dichloro-, ethyl ester, monohydrobromide (9CI) (CA INDEX NAME)



● HBr

L4 ANSWER 20 OF 20 ZCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1979:405248 ZCAPLUS

DOCUMENT NUMBER: 91:5248

TITLE: Alkyl 5,6-dichloro-3,4-dihydro-2(1H)-iminoquinazoline-3-acetate hydrohalides

INVENTOR(S): Jenks, Thomas A.; Beverung, Warren N., Jr.; Partyka, Richard A.

PATENT ASSIGNEE(S): Bristol-Myers Co., USA

SOURCE: U.S., 8 pp.
CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 4146718 | A | 19790327 | US 1978-894464 | 19780410 |
| CA 1109067 | A1 | 19810915 | CA 1979-324838 | 19790403 |
| FI 7901125 | A | 19791011 | FI 1979-1125 | 19790405 |
| FI 66616 | B | 19840731 | | |
| FI 66616 | C | 19841112 | | |
| DK 7901447 | A | 19791011 | DK 1979-1447 | 19790406 |
| DK 156062 | B | 19890619 | | |
| DK 156062 | C | 19891106 | | |
| AU 7945889 | A | 19791018 | AU 1979-45889 | 19790406 |

| | | | | |
|---|---|---|---|---|
| AU 527748 | B2 | 19830324 | | |
| FR 2422649 | A1 | 19791109 | FR 1979-8770 | 19790406 |
| FR 2422649 | B1 | 19830729 | | |
| GB 2018765 | A | 19791024 | GB 1979-12354 | 19790409 |
| GB 2018765 | B | 19820804 | | |
| HU 21861 | A2 | 19820227 | HU 1979-BI586 | 19790409 |
| HU 179424 | B | 19821028 | | |
| HU 28466 | A2 | 19831228 | HU 1982-177 | 19790409 |
| HU 187562 | B | 19860128 | | |
| SU 1120923 | A3 | 19841023 | SU 1979-2751007 | 19790409 |
| BE 875475 | A1 | 19791010 | BE 1979-194524 | 19790410 |
| SE 7903198 | A | 19791011 | SE 1979-3198 | 19790410 |
| SE 445217 | B | 19860609 | | |
| SE 445217 | C | 19860918 | | |
| NL 7902825 | A | 19791012 | NL 1979-2825 | 19790410 |
| NL 191182 | B | 19941003 | | |
| NL 191182 | C | 19950301 | | |
| DE 2914494 | A1 | 19791018 | DE 1979-2914494 | 19790410 |
| DE 2914494 | C2 | 19890720 | | |
| JP 54135794 | A | 19791022 | JP 1979-42626 | 19790410 |
| JP 02033035 | B | 19900725 | | |
| ZA 7901727 | A | 19800528 | ZA 1979-1727 | 19790410 |
| CH 639079 | A5 | 19831031 | CH 1979-3388 | 19790410 |
| CA 1137474 | A2 | 19821214 | CA 1981-381570 | 19810710 |
| DK 8200767 | A | 19820222 | DK 1982-767 | 19820222 |
| DK 150605 | B | 19870413 | | |
| DK 150605 | C | 19871207 | | |
| FI 8300150 | A | 19830117 | FI 1983-150 | 19830117 |
| FI 71931 | B | 19861128 | | |
| FI 71931 | C | 19870309 | | |
| SE 8404061 | A | 19840810 | SE 1984-4061 | 19840810 |
| SE 454990 | B | 19880613 | | |
| SE 454990 | C | 19880922 | | |
| DK 8603166 | A | 19860703 | DK 1986-3166 | 19860703 |
| DK 154838 | B | 19881227 | | |
| DK 154838 | C | 19890710 | | |
| JP 02022276 | A | 19900125 | JP 1989-137585 | 19890601 |
| JP 03012066 | B | 19910219 | | |

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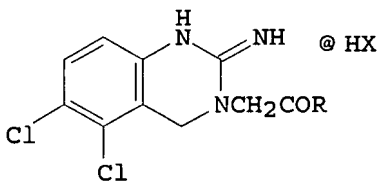
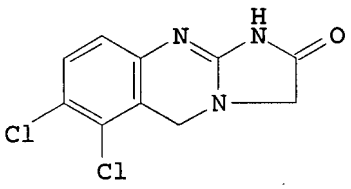
|---|---|---|---|
| PRIORITY APPLN. INFO.: | US 1978-894464 | A | 19780410 |
| | CA 1979-324838 | A3 | 19790403 |
| | FI 1979-1125 | A | 19790405 |
| | DK 1979-1447 | A | 19790406 |

OTHER SOURCE(S): MARPAT 91:5248

GI




I



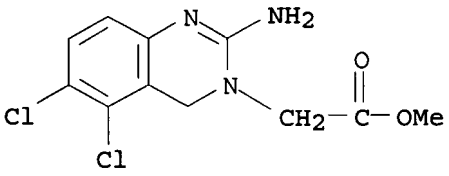

IV

AB The title compds. I (R = alkyl; X = Cl, Br, iodo) were prepared Thus, 2,3,6-Cl2(H2N)C6H2CH2NHCH2CO2Et (II) was cyclized with BrCN to give I (R = Et, X = Br) (III), which was cyclized to give 6,7-dichloro-1,5-dihydroimidazo[2,1-b]quinazoline-2(3H)-one (IV). II was prepared in 5 steps from 1,2,3-Cl3C6H3 and in 5 steps from 4-chloroisatin. The

antiaggregative and antithrombosis activity of II was compared with aspirin, dipyridamole, and sulfinpyrazone.

IT 70380-52-8P 70380-53-9P 70380-54-0P
70380-55-1P 70380-56-2P 70380-57-3P
70381-75-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 70380-52-8 ZCAPLUS
CN 3(4H)-Quinazolineacetic acid, 2-amino-5,6-dichloro-, methyl ester, monohydrobromide (9CI) (CA INDEX NAME)



● HBr

RN 70380-53-9 ZCAPLUS
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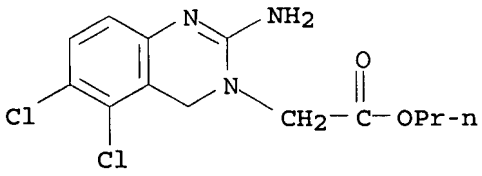

● HBr

RN 70380-54-0 ZCAPLUS
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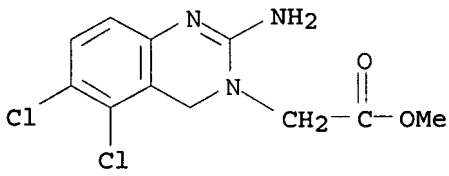

● HCl

RN 70380-55-1 ZCAPLUS
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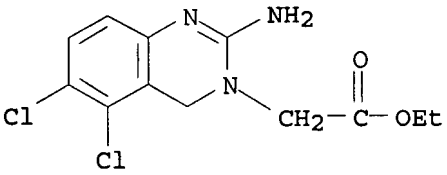

● HCl

RN 70380-56-2 ZCAPLUS
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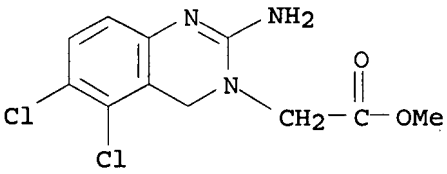

● HI

RN 70380-57-3 ZCAPLUS
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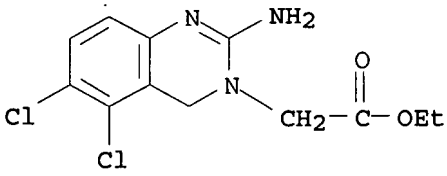
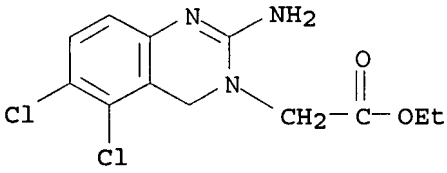


● HI

RN 70381-75-8 ZCAPLUS
CN 3(4H)-Quinazolineacetic acid, 2-amino-5,6-dichloro-, ethyl ester, monohydrobromide (9CI) (CA INDEX NAME)



● HBr

10/ 541,535

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L2 9 S L1 SAMPLE
L3 166 S L1 FUL

FILE 'ZCAPLUS' ENTERED AT 14:11:49 ON 07 MAY 2007
L4 20 S L3

=> log y

| COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION |
|---|---|---|
| FULL ESTIMATED COST | 105.46 | 277.77 |
| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE ENTRY | TOTAL SESSION |
| CA SUBSCRIBER PRICE | -15.60 | -15.60 |

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